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(54) Title: ABSORBENT ARTICLES WITH BUFFER

(57) Abstract: There is described a vaginal article which is adapted to balance the pH of vaginal mucosa and/or menses. There is also described a method of treating or alleviating or prophylactically preventing a vaginal disorder which comprises the use of such an article.

ABSORBENT ARTICLES WITH BUFFER

The present invention relates to absorbent articles, e.g. tampons, wipes, etc. and methods of manufacture.

Vaginal problems can occur for a variety of reasons, *inter alia*, transfer of organisms from other body areas, e.g. anus, fingers, etc., from other people, i.e.; during sexual intercourse, from contact with materials, e.g. toilet seat, from irritation via textile materials, e.g.; panty gusset, or once a fungal infection is present, it may reappear if the conditions are favourable to re-present the original condition.

The vagina is home to a large number of microbes known as the normal flora. These organisms usually cause no illness in a healthy individual. Their presence protects the individual from foreign microorganisms and overgrowth of pre-existing organisms that can lead to pathogenic states. They do this by taking up available attachment sites and by producing antimicrobial compounds such as hydrogen peroxide and bacteriocin like substances (Boris s et al 2000).

Age related physiological changes affect the composition of the normal flora. Prior to puberty the conditions within the vagina favour the growth of species such as staphylococci, streptococci, diphtheroids and some coliforms (Talaro, K., et al 1996). A pH of 7 is normal in a pre-pubescent girl who would produce little oestrogen. At puberty production of oestrogen increases and induces secretion of glycogen from vaginal mucosal cells. *Lactobacillus aerophilus* then begins to predominate and ferment the glycogen resulting in the normal acid pH (3.8-4.2 (Plourd,D.,M., 1997)) that prevents overgrowth by other commensuals. Nagy et al 1992 believed that the acidic pH helps to maintain the balance of the vagina by increasing the binding capacity of lactobacilli. At menopause the flora returns to a similar composition and therefore the pH that exists at prepuberty. There is a relationship between increased vaginal pH and abnormal vaginal secretions (Roupas, A., et al 1985).

Vaginal thrush affects 20 million women each year. It is particularly common in women taking the contraceptive pill or antibiotics (particularly tetracycline), during pregnancy, and in diabetics. An increased hormone level in pregnant women and those taking oestrogen containing contraceptive pills raises vaginal pH. This provides an environment suitable for fungal growth and nourishment such as *Candida albicans* the causative agent of thrush. *Candida albicans* is a fungus that infects the mucous membranes of the vagina. Though the organism is a component of the normal commensuals population, an increase in its concentration can lead to the pathogenic condition known as thrush. Overgrowth can occur if vaginal pH rises, competing commensuals then diminish allowing the load of *Candida spp.* to increase substantially. It causes an uncomfortable vaginitis in those suffering from this condition. A vaginal discharge may occur accompanied by dysuria and urethritis.

Bacterial vaginosis was first reported in 1995 and it is currently the most prevalent cause of infectious vaginitis (Gonzalez Pedraza Aviles A et al,1999). Bacterial vaginal infections occur when the usually predominant lactobacillus population are replaced with a mixed predominantly anaerobic population including *Gardnerella vaginalis* a normal commensual of the vagina (Spiegal C.,A., et al 1983), *Bacterioides spp., Eubacte spp* and *mycoplasma* (Hill GB et al 1984). These infections are common and are associated with a pH greater than 4.5 (Wang, J, 2000).

Treatment leading to dominance by Lactobacilli results in a lowered pH and therefore the absence of the bacterial infection. It is important to treat BV due to its association with a number of complications such as cervicitis, endometritis, pelvic inflammatory disease and a possible link with intraepithelial neoplasia (Georgijevic, A., et al 2000).

Conventional absorbent tampons such as catamenial tampons normally comprise an absorbent material of general cylindrical shape, and can be formed from a length of absorbent material comprising hydrophilic fibres such as cellulosic fibres by compressing the material longitudinally or laterally or both. Tampons formed by

lateral compression and in particular radial compression have the advantage of being capable of expanding laterally in use thereby inhibiting the leakage of menses around the inserted tampon. A typical method of forming radially compressed tampons is given in British Patent No. 1082770.

The pH level of vaginal mucosa is prepubescent or postmenopausal females is generally around neutral i.e. pH 7. However, we have recently established that the pH of vaginal mucosa in a female may vary depending upon the stage of the menstrual cycle. In females experiencing the menstrual cycle the pH of the vaginal mucosa is generally from pH 4 to pH 4.5. However, since the pH of blood is generally higher than the pH of vaginal mucosa, during the period of menstruation, when the lining of the uterus is shed, the pH of the vagina. Thus, the pH of vaginal mucosa may increase. It is thought that this may be due to the presence of quantities of blood in the mucosa which will generally have a pH of 7.

However, this change in pH of the vaginal mucosa gives rise to a number of problems. Thus, for example, the change from a significantly acidic pH to a neutral pH means that a female can be prone to infections and/or other disorders.

It is also understood that HIV appears to survive best at a neutral pH, studies have shown that both cell-free HIV and HIV-infected cells are rapidly inactivated at pH levels below 4.5 and 5.5 respectively, as are several harmful bacteria including those causing gonorrhoea and bacterial vaginosis. Following unprotected vaginal intercourse, semen raises the pH of the vagina and keeps it elevated at around 5.5 to 7.0 for at least two hours. It is believed that this rise in pH facilitates the survival of sperm but also the survival of any HIV that may be present in the semen.

Following our discovery of these changes in the pH of vaginal mucosa, we have now developed a vaginal article e.g. a tampon which attempts to mitigate the problems of pH variation. Vaginal hygiene wipes are known, but these generally have a pH of greater than about 5.5.

Thus according to the invention we provide a vaginal article which is adapted to balance the pH of vaginal mucosa and/or menses.

The vaginal article may be a feminine wipe. However, preferably, the vaginal article of the invention may be an intra vaginal article, for example a tampon.

Thus, the article of the invention may be provided with a pH control agent. Preferentially, the pH control agent is an acid-buffering agent, which should be a non-toxic, non-irritating acidic material which release protons. A variety of acid-buffering agents may be used, preferably the acid-buffering agent is one or more low molecular weight organic or inorganic acids, and salts thereof, high molecular weight polymeric acids or ion exchange resins and fibres in the hydrogen form. Most preferably the acid-buffering agent is selected from the group including citric acid and sodium citrate. Preferably the pH control agent is one which reduces the pH to a range of from 3.5 to 5.5, preferably from 3.8 to 4.2 and most preferably to about pH 4.

During menstruation a conventionally tampon is worn for a period of from 4 to 8 hours. Furthermore, since, as hereinbefore described, following intercourse, vaginal pH is elevated for a period of about two hours, an especially preferred pH control agent is one which reduces the vaginal pH to the range described above, e.g. 3.5 to 5.5, and maintains that reduced vaginal pH for several hours. Preferably, the reduction in vaginal pH is maintained for at least 2 hours and more preferably for a range between 4 to 8 hours.

The acid-buffering agent may be in a variety of forms, such a hydrogel or a thin film. Certain hydrogels which may be mentioned are ACIDFORM and Aci-Jel, both of which are currently undergoing clinical trials.

Thus, the tampon may be provided with a coating of a pH control agent or, alternatively, the tampon of the invention may be impregnated with a pH control

agent. Of course, it is within the scope of the present invention to provide a tampon which is impregnated, or partially impregnated and carries a coating of a pH control agent. In a yet further alternative the tampon of the invention may utilise a packaging system such as that disclosed in our co-pending application No. GB 0031655.4. Alternatively, the fibres of the tampon may be treated to render them pH balancing. Such treatment may, for example, include pre-treatment of the fibres prior to them being compressed into a tampon. In a further alternative, the nature of the fibres used may be selected such that they possess a pH balancing effect.

In a further embodiment of the invention the tampon may also be provided with a medicament. A variety of medicaments may be chosen. In particular, a group of antimycotic (antifungal) drugs known as imidazoles have been found to be effective in the treatment of Candida species. Four main drugs are used; clotrimazole, miconazole, econazole and ketoconazole. They work by blocking production of ergosterol, the main sterol in the fungal cell membrane. This ultimately effects the action of membrane-associated enzymes so that replication of the fungus is inhibited. It also prevents the non-pathogenic form of the microbe developing into the invasive form (hyphae). The drugs produce cell necrosis by inhibiting peroxidase enzymes. Development of resistance to the imidazoles is rare.

Clotrimazole interferes with amino acid transport into the organism by attacking the cell membrane. It is a drug of choice for treatment of candidiasis of the vagina. Adverse effects can occur on application to the skin and include stinging, erythema, pruritis, peeling. The incidence however is low. Intravaginal administration can be associated with a burning sensation and lower abdominal cramps. This drug is available as a cream or tablet for intravaginal use and can also be applied topically.

Miconazole is used topically, but rarely systemically due to toxicity issues. Systemic use is by intravenous infusion and is associated with fever, nausea, and a rash. It also can enhance the action of oral anticoagulants leading to haemorrhage. Around 15%

of C. albicans are resistant to clotrimazole and miconazole. Recurrent infections can be treated with fluconazole.

Econazole is available for topical application. Adverse effects include burning and itching sensations, though these have been observed in just 3% of users. Less than 1% of topical econazole is absorbed. A 1% cream is applied twice a day for 2 weeks.

Ketoconazole can be administered orally to treat superficial mycoses. The toxicity associated with the drug means that its' use is only advised for those mycoses which have not responded to topical agents.

Other treatments include Nystatin, a polyene antibiotic. It is used solely to treat candidiasis by topical, intravaginal and oral routes. Significant absorption has not been observed with any of these routes. Intravaginal application of the drug is by administration of a vaginal tablet. Dosage ranges between 100,000 – 200,000 units daily for a period of two weeks. Adverse effects reported by Lehne et al are limited to oral Nystatin (occasionally causes gastrointestinal disturbances) and topical application (can cause local irritation).

Treatment of BV usually consists of metronidazole or clindamycin by mouth or intravaginally (Georgijevic A., et al 2000) (Wang, J 2000) (Gonzalez Pedraza Aviles A., et al 1999). Hanson et al compared metronidazole in two forms in 2000. Two groups were involved in the trial, one was treated with an oral dose of metronidazole and the other group treated with metronidazole vaginal gel. The efficacy in both treatment groups was comparable. The application of 0.75% vaginal gel twice daily for 5 days was associated with fewer gastrointestinal complaints than standard oral treatment. In the case of recurrent bacterial vaginosis, Winceslaus et al (1996) found that a single vaginal washout with 3% hydrogen peroxidase cleared symptoms of 78% of those involved in the trial.

Liposomes made of phosphatidylcholine have been tested for their ability to act as a carrier for drug delivery to the vagina in the treatment of vaginal infections. In vitro and in situ studies carried out by Pavelic et al confirmed the ability of liposomes to act as a carrier system for vaginal delivery.

A new vaginal formulation called ACIDFORM has been designed as an antimicrobial /contraceptive product. It is acid-buffering and can therefore maintain the acidic environment of the vagina (McLean N., W., et al 2000). Garg et al found ACIDFORM to be more effective and bioadhesive than Aci-Jel (a commercial acid buffering vaginal product)

Another option of treating vaginal bacteriosis is to use Lactobacillus isolates to recolonise the vagina and therefore lower and maintain the acidic pH McLean, N., W., et al 2000).

In a yet further aspect of the invention the tampon may also be provided with a lubricant, e.g. in the form of a coating, for example, on a shoulder portion of the tampon, provided it is sufficient to allow insertion of the tampon into the vagina without undue discomfort.

The lubricants used in the invention can be any of the lubricants which are suitable for coating absorbent tampons to reduce the frictional drag thereof during insertion into the vagina.

Preferred lubricants for use in the invention comprise a water soluble polymer. Such a water soluble polymer lubricant coating on a tampon of the invention in use can, on contact with the vagina wall, absorbed moisture and become highly lubricious thus further enhancing the lubricant nature of the coating. Furthermore a water soluble polymer lubricant coating on a tampon after insertion may eventually be dissolved by fluids present in the vagina from the surface of the tampon thereby making the surface available for absorbing menses.

The absorbent tampon used in the invention can be any of the absorbent tampons conventionally used for catamenial purposes which has a rounded insertion end and is capable of expanding laterally in use. Suitable methods of forming a rounded end on a absorbent include those disclosed in British Patent No. 1046066. The rounded insertion end can be hemispherical, rounded conical or alike rounded tapered shape. Favoured tampons of the invention comprise a spirally wound fleece of absorbent cellulosic fibres which has been compressed radially for example between compression dies.

Suitable methods of making tampons comprising spirally wound fleece include those disclosed in British Patent No. 1098400. Suitable methods of forming tampons by radially compressing absorbent material include those disclosed in British Patent 1082770.

The absorbent tampons of the invention will be suitable for digital use. The tampons can be packed within a wrapper of water impermeable film such as moisture proof coated cellulose film, polypropylene film or polypropylene film. The film can conventionally be closed by a breakable seal for example a heat seal over insertion end to enable the tampon to be inserted via the seal from the wrapper into the vagina. Suitable wrappers of this type are disclosed in British Patent No. 1305472. Alternatively, as previously mentioned, a tampon, which may optionally be uncoated and/or unimpregnated, may utilise a packaging system such as that disclosed in our co-pending application No. PCT/GB01/05622.

The tampon within the wrapper can favourably be sterile. Suitable methods of sterilising include gamma and electron beam irradiation methods.

The materials used in the method of the invention can be the materials described hereinbefore in relation to the tampon of the invention.

In the method of the invention pH control agent may be provided on the tampon by any suitable method. Suitable methods include, but shall not be limited to, adhering a preformed solid film of the lubricant to the tampon by for example solvent or heat and coating the lubricant in liquid form for example as a hot melt or as a solution onto the tampon by spraying or other coating method.

In a method of the invention which comprises spraying, the lubricant can be sprayed as a band on the shoulder portion of the insertion of the tampon by controlling the width of the spray and rotating the spray head or the tampon under the spray head. In such methods the surface of the main body of the tampon which is adjacent to the shoulder portion or region can advantageously be surrounded by a cylindrical member to inhibit the lubricant being coated on the side surface of the tampon. The cylindrical member can favourably be part of the outer wrap of the tampon before it is sealed.

A wide variety of non-toxic, non-irritating acidic materials which release protons can serve as pH control agents. For instance, these materials can be low molecular weight organic or inorganic acids, high molecular weight polymeric acids or ion exchange resins and fibres in the hydrogen form. Particular pH control agents which may be mentioned include citric acid and sodium citrate.

The deposition of the active ingredient of the pH control agent onto the skin of the user can occur both through dry and/or wet transfer within the absorbent article environment.

The absorbent article of the present invention can include the pH control agent in at least a portion of any of its interior component parts in an amount sufficient to maintain prolonged natural skin pH.

It is particularly preferred that a component part of the absorbent article which comes into substantial contact with the vaginal mucosa of the intended user includes the pH

control agent. In another preferred embodiment, the pH control agent can be included in at least a portion of the absorbent core and at least a portion of the topsheet or tissue layer, although any single component part or combination of component parts is within the scope of the present invention.

Preferably, the pH control agent is present in an amount of at least about 1% by weight, preferably from about 1% by weight to about 10% by weight, and more preferably about 2% by weight of the pH control agent, based on the total weight of the tampon. In a particular embodiment, which may be mentioned, the pH control agent may comprise about 2% by weight citric acid, based on the total weight of the tampon.

According to a further aspect of the invention we provide a method of manufacturing a tampon as hereinbefore described characterised in that the method comprises adhering, coating or impregnating a pH control agent onto or into a vaginal article.

A variety of processes may be used in the method of the invention. Thus, in one aspect, a preformed solid film of an acid buffer may be applied to the tampon by, for example, solvent or heat. Alternatively, the acid buffer may be applied in liquid form, as a hot melt or as a solution onto the tampon by spraying or other coating method, including, for example, kiss-coating.

One method which may be mentioned is that of spraying the acid buffer as a hot melt onto the shoulder area of the tampon.

Preferably, the pH control agent is applied to the treated portion of the component part of the absorbent article as an aqueous solution comprising the pH control agent.

In another aspect the invention provides a method of treating or alleviating or prophylactically preventing a vaginal disorder which comprises the use of a vaginal article as hereinbefore described.

Thus the use of the article of the invention, and especially the tampon of the invention may, in lowering vaginal pH, also act as a spermicidal agent and/or a means of preventing or alleviating transmission of HIV. Therefore according to a further aspect of the invention we provide a method of treating, alleviating or preventing the transmission of HIV which comprises the use of a tampon of the invention.

The use of the tampon of the invention may also be advantageous as a means of preventing or alleviating the transmission of other sexually transmitted diseases. Such diseases may include, but shall not be limited to those resulting from a viral disease, a bacterial disease, a protozoal disease and/or a fungal disease. When the disease is a viral disease, it may be selected from HIV and genital herpes. When the STD is a fungal disease, it may be, for example, *Candida*, e.g. *Candida albicans*. In a further alternative aspect of the invention, the STD may be a bacterial disease, such as chlamydia.

Thus, specific STDs, which may be mentioned, are bacterial vaginosis, chlamydia, genital herpes, genital warts, gonorrhoea, syphilis, trichomoniasis and *Candida*.

In the method of the invention a tampon may be used alone or in conjunction with a hygienic wipe as hereinbefore described.

Thus according to a further aspect of the invention we provide a kit comprising a wipe and a tampon as hereinbefore described.

The invention will now be illustrated by way of example only.

Example 1

ATO:	INCI ADOPTED NAME:	RAW MATERIAL:	RAW MATERIAL FUNCTION:	PERCENT:
ATO000	Aqua (100%)	PURIFIED WATER	Vehicle	75.495000
ATO631	Propylene Glycol (100%)	MONOPROPYLENE GLYCOL	Humectant / Solvent	1.000000
ATO513	Sodium Methylparaben (100%)	NIPAGIN M SODIUM	Preservative	0.100000
ATO552	Sodium Propylparaben (100%)	NIPASOL M SODIUM	Preservative	0.040000
ATO342	Glycerin (100%)	PRICERINE 9091 / GLYCERIN BP/USP / GLYCERIN (VEG)	Humectant	20.000000
ATO761	Sodium Citrate (100%)	TRISODIUM CITRATE	Buffering Agent	0.500000
ATO544	Disodium EDTA (100%)	VERSENE NA2 CRYSTALS / NERVANAID BA2 POWDER	Chelating Agent	0.150000
ATO555	Hydroxyethylcellulose (100%)	NATROSOL 250 HX-PHARM	Thickener	2.133000
ATO143	2-Bromo-2-Nitropropane-1,3-Diol (100%)	MYACIDE PHARMA BP / BRONOPOL	Preservative	0.025000
ATO185	Citric Acid (100%)	CITRIC ACID	pH Adjuster	0.557000
			TOTAL	**100.0000**

Example 2

ATO:	INCI ADOPTED NAME:	RAW MATERIAL:	RAW MATERIAL FUNCTION:	PERCENT:
ATO000	Aqua (100%)	PURIFIED WATER	Vehicle	75.495000
ATO631	Propylene Glycol (100%)	MONOPROPYLENE GLYCOL	Humectant / Solvent	1.000000
ATO513	Sodium Methylparaben (100%)	NIPAGIN M SODIUM	Preservative	0.100000
ATO552	Sodium Propylparaben (100%)	NIPASOL M SODIUM	Preservative	0.040000
ATO342	Glycerin (100%)	PRICERINE 9091/ GLYCERIN BP/USP / GLYCERIN (VEG)	Humectant	20.000000
ATO463	Lactic Acid (88%), Aqua (12%)	PURAC SP88	Humectant	0.390400
D0317	Sodium Lactate (50%), Aqua (50%)	Sodium Lactate		0.666600
ATO544	Disodium EDTA (100%)	VERSENE NA2 CRYSTALS / NERVANAID BA2 POWDER	Chelating Agent	0.150000
ATO555	Hydroxyethylcellulose (100%)	NATROSOL 250 HX-PHARM	Thickener	2.133000
ATO143	2-Bromo-2-Nitropropane-1,3-Diol (100%)	MYACIDE PHARMA BP / BRONOPOL	Preservative	0.025000
			TOTAL	100.0000

Claims

1. A vaginal article which is adapted to balance the pH of vaginal mucosa and/or menses.

2. A vaginal article according to claim 1 characterised in that the article is a wipe.

3. A vaginal article according to claim 1 characterised in that the article is a tampon.

4. A vaginal article according to claim 1 characterised in that the article is provided with a pH control agent.

5. A vaginal article according to claim 4 characterised in that the pH control is one which reduces the pH to a range of from 3.5 to 5.5.

6. A vaginal article according to claim 5 characterised in that the pH control is one which reduces the pH to a range of from 3.8 to 4.2 .

7. A vaginal article according to claim 6 characterised in that the pH control is one which reduces the pH to about pH 4.

8. A vaginal article according to claim 5 characterised in that the pH control is one which maintains the reduced vaginal pH for several hours.

9. A vaginal article according to claim 8 characterised in that the pH control is one which one which maintains the reduced vaginal pH for at least 2 hours.

10. A vaginal article according to claim 9 characterised in that the pH control is one which one which maintains the reduced vaginal pH for a range between 4 to 8 hours.

11. A vaginal article according to claim 4 characterised in that the pH control agent is an acid-buffering agent.

12. A vaginal article according to claim 11 characterised in that the acid-buffering agent is a non-toxic, non-irritating acidic material which release protons.

13. A vaginal article according to claim 11 characterised in that the acid-buffering agent is one or more low molecular weight organic or inorganic acids and salts thereof, high molecular weight polymeric acids or ion exchange resins and fibres in the hydrogen form.

14. A vaginal article according to claim 13 characterised in that the acid-buffering agent is selected from the group including citric acid and sodium citrate.

15. A vaginal article according to claim 11 characterised in that the acid-buffering agent is in the form of a hydrogel.

16. A vaginal article according to claim 15 characterised in that the acid-buffering agent is selected from ACIDFORM and Aci-Jel.

17. A vaginal article according to claim 4 characterised in that the article is provided with a coating of a pH control agent.

18. A vaginal article according to claim 4 characterised in that the article is impregnated with a pH control agent.

19. A vaginal article according to claim 1 characterised in that the article is also provided with a medicament.

20. A vaginal article according to claim 1 characterised in that the medicament is an antimycotic.

21. A vaginal article according to claim 20 characterised in that the antimycotic is an imidazole.

22. A vaginal article according to claim 21 characterised in that the imidazole is selected from the group including clotrimazole, miconazole, fluconazole, econazole, metronidazole and ketoconazole.

23. A vaginal article according to claim 20 characterised in that the medicament is selected from the group including metronidazole and clindamycin.

24. A vaginal article according to claim 1 characterised in that the article is also provided with a lubricant.

25. A vaginal article according to claim 4 characterised in that the weight per unit area of the pH control agent on or in the article is from 0.01 to 0.25g/cm^2.

26. A vaginal article according to claim 1 characterised in that the article is packed within a wrapper of impermeable film.

27. A vaginal article according to claim 26 characterised in that the impermeable film is selected from a coated cellulose film, polypropylene film or polypropylene film.

28. A vaginal article according to claim 1 characterised in that the article is housed in a packaging system such as that disclosed in co-pending application No. PCT/GB01/05622.

29. A vaginal article according to claim 1 characterised in that the pH control agent is in at least a portion of any of the interior component parts of the article.

30. A vaginal article according to claim 4 characterised in that the pH control agent is present in the article in an amount of from about 1% w/w to 10% w/w.

31. A method of treating or alleviating or prophylactically preventing a vaginal disorder which comprises the use of an article of the invention.

32. A method of treating, alleviating or preventing the transmission of HIV which comprises the use of an article according to claim 1.

33. A method according to claim 32 characterised in that the article is a tampon.

34. A method according to claim 32 characterised in that the disorder is a sexually transmitted disease.

35. A method according to claim 34 characterised in that the sexually transmitted disease is selected from one or more of a viral disease, a bacterial disease, a protozoal disease and/or a fungal disease.

36. A method according to claim 35 characterised in that the sexually transmitted disease is selected from one or more of bacterial vaginosis, chlamydia, genital herpes, genital warts, gonorrhoea, syphilis, trichomoniasis and *Candida*.

37. A method according to claim 28 characterised in that the tampon is used in conjunction with a hygienic wipe.

38. A kit comprising a wipe according to claim 2 and a tampon according to claim 3.

39. A method of manufacturing an article according to claim 1 characterised in that the method comprises applying a pH control agent onto or into an article.

40. A method according to claim 39 characterised in that the method comprises spraying the acid buffer as a hot melt onto the shoulder area of the tampon.

41. An article or a method substantially as hereinbefore described with reference to the accompanying examples.

P36723WO.2

INTERNATIONAL SEARCH REPORT

tional Application No
PCT/GB 02/05829

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L15/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, MEDLINE, EMBASE, BIOSIS, CHEM ABS Data, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 130 356 A (HENKEL KGAA) 9 January 1985 (1985-01-09) claims 1-3; examples 1,2,4	1-41
X	US 3 067 745 A (BURGENI ALFRED A ET AL) 11 December 1962 (1962-12-11) column 5, line 5 - line 8; examples I-III	1-41
X	US 4 309 997 A (DONALD JACK W) 12 January 1982 (1982-01-12) column 3, line 1 - line 4	1-41
X	US 4 634 438 A (MARINI INGO G ET AL) 6 January 1987 (1987-01-06) claims 1-3,6; examples 8,9	1-41

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 March 2003	31/03/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pilling, S

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

tional Application No
PCT/GB 02/05829

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Section Ch, Week 198627 Derwent Publications Ltd., London, GB; Class B05, AN 1986-174734 XP002235005 & SE 8 404 940 A (ANDERSCH B), 4 April 1986 (1986-04-04) abstract	1-41
X	DATABASE WPI Section Ch, Week 199953 Derwent Publications Ltd., London, GB; Class B07, AN 1999-618267 XP002235006 & RU 2 113 183 C (MOLCHANOV O L), 20 June 1998 (1998-06-20) abstract	1-41
X	US 4 369 773 A (CHVAPIL MILOS) 25 January 1983 (1983-01-25) abstract column 2, line 18 - line 25	1-41
X	US 4 585 782 A (PLEMPEL MANFRED ET AL) 29 April 1986 (1986-04-29) column 1, line 14 - line 55; claims 4,5; examples 1-3	1-41
X	US 5 466 463 A (FORD LARRY C) 14 November 1995 (1995-11-14) column 5, line 21 - line 47	1-41
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X	US 5 617 877 A (MOENCH THOMAS R ET AL) 8 April 1997 (1997-04-08) abstract	1-41
X	WO 90 14832 A (CURATEK PHARMACEUTICALS) 13 December 1990 (1990-12-13) page 10, line 10 - line 15 page 17, line 1 - line 11; claim 1; examples 1-12	1-41

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-4 and Claims 11-41 in part

The definition in present Claim 1 of a "A vaginal article which is adapted to balance the pH of the vaginal mucosa and/or menses" is vague and unclear (Article 6 PCT). In this regard, Claim 1 appears to define an article which may be used intravaginally and has some form of buffering capability. Nevetheless, the nature of the buffering, i.e. the desired pH range is undefined. Thus, the present Searching Authority considers that present Claims 1 to 4 and claims dependent thereon are unclear within the meaning of Article 6 PCT. Consequently a full and meaningful search of Claims 1 to 4 and claims dependent thereon is impossible.

Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely an article which may be used intravaginally and has a pH control agent which is capable of rendering the pH of the vagina and the menses to a range of from 3.5 to 5.5 (see present Claim 5).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 02/05829

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-4 and Claims 11-41 in part
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

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PCT/GB 02/05829

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